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10/822,235	04/09/2004	Susan Gould-Fogerite	BSZ-049	1705

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EXAMINER	
WHITEMAN, BRIAN A	
ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 07/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/822,235	GOULD-FOGERITE ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-63* is/are pending in the application.

4a) Of the above claim(s) *7,14-63* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 April 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/4/05*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *5/8/06*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Non-Final Rejection

Claims 1-63 are pending.

The amendment to the specification and the response to the election/restriction filed on 5/11/06 is acknowledged by the examiner. In view of the instant office action and interview summary (5/8/06), the election/restriction mailed on 4/11/06 is vacated.

There is a problem with the sequence listing submitted on 5/11/06. See Raw Sequence Listing Error Report for further explanation. A complete reply to the instant office action must include a response to the error report.

Election/Restrictions

During a telephone conversation with Danielle Herritt on 5/8/06 a provisional election was made without traverse to prosecute the invention of Group II, claims 1-4, 6, and 8-13. Affirmation of this election must be made by applicant in replying to this Office action. A cancer protein, a fungus protein, a bacterial protein, an abnormal cellular protein, and a normal cellular protein in claim 6 and claims 7 and 14-63 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-4, 6, and 8-13, drawn to an siRNA-cochleate composition comprising a cochleate and an siRNA associated with the cochleate, wherein the siRNA

mediates interference against a target mRNA expressing a cancer protein, classifiable in class 514, subclass 44.

II. Claims 1-4, 6, and 8-13, drawn to an siRNA-cochleate composition comprising a cochleate and an siRNA associated with the cochleate, wherein the siRNA mediates interference against a target mRNA expressing a viral protein (HIV protein), classifiable in class 514, subclass 44.

III. Claims 1-4, 6, and 8-13, drawn to an siRNA-cochleate composition comprising a cochleate and an siRNA associated with the cochleate, wherein the siRNA mediates interference against a target mRNA expressing a fungal protein, classifiable in class 514, subclass 44.

IV. Claims 1-4, 6, and 8-13, drawn to an siRNA-cochleate composition comprising a cochleate and an siRNA associated with the cochleate, wherein the siRNA mediates interference against a target mRNA expressing a bacterial protein, classifiable in class 514, subclass 44.

V. Claims 1-4, 6, and 8-13, drawn to an siRNA-cochleate composition comprising a cochleate and an siRNA associated with the cochleate, wherein the siRNA mediates interference against a target mRNA expressing an abnormal cellular protein, classifiable in class 514, subclass 44.

VI. Claims 1-4, 6, and 8-13, drawn to an siRNA-cochleate composition comprising a cochleate and an siRNA associated with the cochleate, wherein the siRNA mediates interference against a target mRNA expressing a cellular protein, classifiable in class 514, subclass 44.

VII. Claim 7, drawn to an siRNA-cochleate composition comprising a cochleate and an siRNA associated with the cochleate and further comprising a second siRNA directed against a second target mRNA, classifiable in class 514, subclass 44.

VIII. Claims 14-24, drawn to a method of treating a subject having a disease or a disorder associated with expression of a target mRNA comprising administering to a subject an siRNA-cochleate composition, classifiable in class 424, subclass 93.2.

NOTE: Claim 24 lists numerous diseases and disorders that would require the examiner to place each disease or disorder into a separate, which would result in over 100 groups. If applicants elect group VIII, applicants are further required to elect a specific disease or disorder from claim 24. Each disease or disorder is unrelated because each disease requires a different subject and different target mRNA. It would be an undue burden on the examiner to search every disease or disorder listed in the claims because each disease or disorder requires a distinct subject. This is not a species election.

IX. Claims 25-33, drawn to a method of forming a siRNA-cochleate composition comprising precipating a liposome and a siRNA, classifiable in class 424, subclass 450.

X. Claims 34-42, drawn to a morpholino-cochleate composition comprising a cochleate and a morpholino oligonucleotide associated with the cochleate, classifiable 536, class 23.1.

XI. Claims 43, drawn to a morpholino-cochleate composition comprising a cochleate and a morpholino oligonucleotide associated with the cochleate and a second

morpholino oligonucleotide directed against the synthesis of the protein or a second protein, classifiable 536, class 23.1.

XII. Claims 44-61, drawn to a method of administering a morpholino oligonucleotide to a host comprising administering a cochleate and a morpholino oligonucleotide associated with the cochleate, classifiable 424, class 93.2.

XIII. Claims 62 and 63, drawn to a method of treating a subject having a disease or a disorder associated with expression of a target mRNA comprising administering to a subject an morpholino-cochleate composition and an siRNA composition, classifiable in class 514, subclass 44.

NOTE: Claim 63 lists numerous diseases and disorders that would require the examiner to place each disease or disorder into a separate, which would result in over 100 groups. If applicants elect group XIII, applicants are further required to elect a specific disease or disorder from claim 63. Each disease or disorder is unrelated because each disease requires a different subject and different target mRNA. It would be an undue burden on the examiner to search every disease or disorder listed in the claims because each disease or disorder requires a distinct subject. This is not a species election.

The inventions are distinct, each from the other because of the following reasons:

Inventions I-VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions the inventions are unrelated because each invention has a different mode of operation and effect.

The inventions are not coextensive because each invention requires targeting an mRNA from a structurally different protein.

Inventions VII and I-VI are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the target mRNA expresses a protein can be selected from a viral protein, a bacterial protein, fungal protein, cancer protein, cellular protein as recited in Inventions I-VI. The subcombination has separate utility such as delivering the composition to a cell in vitro. Furthermore, it would be an undue burden on the examiner to search all of the inventions together because the examiner would have to further search a composition with two siRNAs and a composition comprising one siRNA.

Inventions I-VI and VIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the composition of groups I-VI can be used to make a composition with several siRNAs as opposed to its use in being delivered to a host.

Searching the inventions of Groups I-VI and VIII together would impose serious search burden. The inventions of Groups I-VI and VIII have a separate search status in the art as shown by their different classifications. Moreover, in the instant case, the search for the composition

and the method of using the composition are not coextensive. Prior art, which teaches the composition, would not necessarily be applicable to the method of using the composition. Moreover, even of the composition were known, the method of using the composition may be novel and unobvious in view of the preamble or active steps.

Inventions VII and VIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are unrelated because the method of Group VIII does not require the composition of group VII.

Searching the inventions of Groups VII and VIII together would impose serious search burden. The inventions of Groups VII and VIII have a separate search status in the art as shown by their different classifications. Moreover, in the instant case, the search for the composition and the method of using a different composition are not coextensive. Prior art, which teaches the composition, would not necessarily be applicable to the method of using the composition. Moreover, even of the composition were known, the method of using the composition may be novel and unobvious in view of the preamble or active steps.

Inventions IX and I-VI are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make another and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the process can be used to make the composition set forth in groups I-VI. The product in Groups I-VI can be made by another and materially different process.

Searching the inventions of Groups I-VI and IX together would impose serious search burden. The inventions of Groups I-VI and IX have a separate search status in the art as shown by their different classifications. Moreover, in the instant case, the search for the composition and the method of producing the composition are not coextensive.

Inventions VII and IX are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are unrelated because the process of Group IX does not require the composition of group VII.

Searching the inventions of Groups VII and IX together would impose serious search burden. The inventions of Groups VII and IX have a separate search status in the art as shown by their different classifications. Moreover, in the instant case, the search for the composition and the method of producing another composition are not coextensive.

Invention X and Inventions I-IX are unrelated because the product of group X is not used or otherwise involved in Inventions I-IX.

Invention XI and Inventions I-IX are unrelated because the product of group XI is not used or otherwise involved in Inventions I-IX.

Invention XII and Inventions I-IX are unrelated because the method of group XII is not used or otherwise involved in Inventions I-IX.

Claim 5 link(s) inventions I-VI. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 5. Upon the indication of allowability of the linking claim(s), the restriction requirement as to the linked inventions shall

be withdrawn and any claim(s) depending from or otherwise requiring all the limitations of the allowable linking claim(s) will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104 Claims that require all the limitations of an allowable linking claim will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

Applicant(s) are advised that if any claim(s) including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. In re Ziegler, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Because these inventions are distinct for the reasons given above and the search required for each Group listed above is not required for any other Group listed above and the search for each group is not co-extensive, restriction for examination purposes as indicated is proper.

It would be unduly burdensome for the examiner to search and consider patentability of all of the presently pending claims, a restriction for examination purposes as indicated is proper.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter

of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 § 1.17(h).

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention, which is also disclosed, in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/461,483, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

The term "siRNA" in Instant claims 1-6 and 8-13 does not have written support under 112 first paragraph in application '483. Thus, instant application only has priority to 4/15/03.

Drawings

Color photographs and color drawings are not accepted unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9-11 recite the limitation "the liposomes" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 5, and 8 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Shapiro et al. (US 20030235577). Shapiro teaches producing a composition comprising siRNA molecules (paragraphs 24, 26, and 28). Shapiro teaches that the composition can be delivered with any delivery vector known in the art, including cochleate (paragraph 140).

Claims 1, 5, and 8-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Unger (A18). Unger teaches a composition comprising cochleate vesicles comprising an anionic lipid, a cationic counter ion, a lipid covalently bonded to a polymer and a bioactive agent (columns 1-

2). The bioactive agent can be a double stranded RNA (column 85). The composition may also comprise a targeting ligand (column 43). The lipid can be a derivative of PEI (column 96).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4, 5, and 8-12 are rejected under 35 U.S.C. 103(a) as being obvious over Margolis et al. (A20) taken with Press Clippings-Managing Complexity: Early Days for RNAi (Wess et al.) 2003-03-17, [online], [retrieved on 2006-05-17] Retrieved from compugen using Internet <URL:http:/www.cgen.com/news/articles/article031703.html>.

Margolis teaches

> The vector delivery system of the present invention comprises a lipidic structure called a cochleate precipitate or, simply, a cochleate. The cochleate comprises a multi-layered lipid bilayers structure. The multi-layered lipid bilayer structure generally comprises a membrane phospholipid containing a negatively charged head group and a cation such as calcium (Ca.sup.++). See column 1.

Margolis further teaches that the vector system comprises an antisense sequence (column 5). Margolis teaches adding a protein to facilitate the nucleotide sequence into a host cell (column 14). However, Margolis does not specifically teach using siRNA in the vector system.

However, at the time the invention was made, siRNA give a better response compared to antisense for shutting down protein synthesis from a target gene as taught by Wess.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Margolis taken with Wess, namely to produce the vector system comprising an siRNA associated with the cochleate. One of ordinary skill in the art would have been motivated to combine the teaching because siRNA gives a better response for shutting down protein synthesis from the targeted gene compared to antisense and to improve the delivery of siRNA to cells.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Unger (A18) taken with McSwiggen (US 20030175950). Unger teaches a composition comprising cochleate vesicles comprising an anionic lipid, a cationic counter ion, a lipid covalently bonded to a polymer and a bioactive agent (columns 1-2). The bioactive agent can be a double stranded RNA (dsRNA), also known to one of ordinary skill in the art as siRNA (column 85). However, Unger does not specifically teach that a siRNA that mediates RNA interference against mRNA from HIV.

However, at the time the invention was made, McSwiggen teaches RNA interference mediated inhibition of HIV gene expression using short interfering RNA (page 56). McSwiggen teaches the siRNA are about 21-23 nucleotides long (page 1). Replacing up to four nucleotides on each end of the siRNA is well tolerated (pages 1-4).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Unger taken with McSwiggen, namely to produce siRNA-cochleate, wherein the siRNA mediates RNA interference against HIV mRNA. One of ordinary skill in the art would have been motivated to combine the teaching to improve the delivery of the siRNA to cells.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Unger taken with McSwiggen, namely to produce siRNA-cochleate, wherein the siRNA is about 21-23 nucleotide long. One of

ordinary skill in the art would have been motivated to combine the teaching because siRNA are most active at this length.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Unger taken with McSwiggen, namely to produce siRNA-cochleate, wherein the siRNA comprises at least one substitution. One of ordinary skill in the art would have been motivated to combine the teaching to improve the stability of the siRNA.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Unger taken with McSwiggen, namely to produce siRNA-cochleate, wherein the siRNA comprises at least one mismatch. One of ordinary skill in the art would have been motivated to combine the teaching to improve the stability of the siRNA.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 1 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 6, 14, and 17 of copending Application No. 10/701,364. Although the conflicting claims are not identical, they are not patentably distinct from each other because both set of claims are directed to a composition comprising an siRNA associated with a cochleate.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim 1 is directed to an invention not patentably distinct from claims 1, 6, 14, and 17 of commonly assigned US application 10/701,364. Specifically, for the reasons set forth above under the double patenting section.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned US application, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the

assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Conclusion

Claim 61 in Application 10/822,230 could be used in a provisional obvious double patenting, however, claim 61 is directed to a non-elected species. Thus, if claim 61 is rejoined during the prosecution of '230, then a provisional odp will be required.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, SPE – Art Unit 1635, can be reached at (571) 272-4517.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of

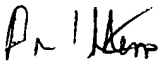
such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Brian Whiteman



BRIAN WHITEMAN
PATENT EXAMINER

Notice to Comply	Application No. 10/822,235	Applicant(s) Susan Gould-Fogerite	
	Examiner B. Whiteman	Art Unit 1635	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set in the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: See Raw sequence listing error report.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the specification**.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (571) 272-2510
For CRF Submission Help, call (571) 272-2501/2583.
PatentIn Software Program Support
Technical Assistance.....703-287-0200
To Purchase PatentIn Software.....703-306-2600

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY

STIC Biotechnology Systems Branch

RAW SEQUENCE LISTING ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 10/822,235 A
Source: IFW16
Date Processed by STIC: 05/17/2006

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.
PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

1) **INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,**
2) **TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY**

FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 571-272-2510; FAX: 571-273-0221

TO **REDUCE** ERRORED SEQUENCE LISTINGS, **PLEASE** USE THE **CHECKER VERSION 4.4.0 PROGRAM**, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:

http://www.uspto.gov/web/offices/pac/checker/chkrnote.htm

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.
Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.
Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (**<http://www.uspto.gov/ebc/efs/downloads/documents.htm>** , **EFS Submission User Manual** - ePAVE)
2. **U.S. Postal Service:** Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
3. **Hand Carry, Federal Express, United Parcel Service, or other delivery service (EFFECTIVE 01/14/05):** U.S. Patent and Trademark Office, Mail Stop Sequence, Customer Window, Randolph Building, 401 Dulany Street, Alexandria, VA 22314

Revised 01/10/06

Raw Sequence Listing Error Summary

ERROR DETECTED	SUGGESTED CORRECTION	SERIAL NUMBER: 10/822,235 A

ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE

1	Wrapped Nucleics Wrapped Aminos	The number/text at the end of each line "wrapped" down to the next line. This may occur if your file was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will prevent "wrapping."
2	Invalid Line Length	The rules require that a line **not exceed** 72 characters in length. This includes white spaces.
3	Misaligned Amino Numbering	The numbering under each 5th amino acid is misaligned. Do not use tab codes between numbers; use **space characters**, instead.
4	Non-ASCII	The submitted file was **not** saved in ASCII(DOS) text, as **required** by the Sequence Rules. **Please ensure your subsequent submission is saved in ASCII text.**
5	Variable Length	Sequence(s)____contain n's or Xaa's representing more than one residue. **Per Sequence Rules, each n or Xaa can only represent a single residue.** Please present the **maximum** number of each residue having variable length and indicate in the <220>-<223> section that some may be missing.
6	PatentIn 2.0 "bug"	A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid sequences(s) _____. Normally, PatentIn would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence. **This applies to the mandatory <220>-<223> sections for Artificial or Unknown sequences.**
7	Skipped Sequences (OLD RULES)	Sequence(s) _____ missing. If intentional, please insert the following lines for **each** skipped sequence: (2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown) (i) SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading) (xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown) This sequence is intentionally skipped Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to **include** the skipped sequences.
8	Skipped Sequences (NEW RULES)	Sequence(s) _____ missing. If **intentional**, please insert the following lines for **each** skipped sequence. <210> sequence id number <400> sequence id number 000
9	Use of n's or Xaa's (NEW RULES)	Use of n's and/or Xaa's have been detected in the Sequence Listing. Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present. In <220> to <223> section, please explain location of **n** or **Xaa**, and which residue **n** or **Xaa** represents.
10	Invalid <213> Response	Per 1.823 of Sequence Rules, the only **valid** <213> responses are: Unknown, ~~Artificial Sequence, or~~ scientific name (Genus/species). <220>-<223> section is **required** when <213> response is Unknown or is Artificial Sequence. (see item 11 below)
11	Use of <220>	Sequence(s) ___ missing the <220> "Feature" and associated numeric identifiers and responses. Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or "Unknown." Please explain source of genetic material in <220> to <223> section or use "chemically synthesized" as explanation. (See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32), also Sec. 1.823 of Sequence Rules
12	PatentIn 2.0 "bug"	Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.
13	Misuse of n/Xaa	"n" can **only** represent a single nucleotide; "Xaa" can **only** represent a single amino acid

IFW16

RAW SEQUENCE LISTING DATE: 05/17/2006
PATENT APPLICATION: US/10/822,235A TIME: 10:44:38

Input Set : A:\SEQLIST - text.txt
Output Set: N:\CRF4\05172006\J822235A.raw

```
  4 <110> APPLICANT: Susan Gould-Fogerite
  5       Raphael Mannino
  6       Patrick Ahl
  7       Gaofeng Shang
  8       Zi Wei Chen
  9       Sara Krause
 11 <120> TITLE OF INVENTION: COCHLEATE COMPOSITIONS DIRECTED AGAINST
 12       EXPRESSION OF PROTEINS
 16 <130> FILE REFERENCE: BSZ-049
 18 <140> CURRENT APPLICATION NUMBER: 10/822,235A
 19 <141> CURRENT FILING DATE: 2004-04-09
 21 <160> NUMBER OF SEQ ID NOS: 16
 23 <170> SOFTWARE: FastSEQ for Windows Version 4.0
```

Does Not Comply
Corrected Diskette Needed
(pg-1,2)

ERRORED SEQUENCES

```
165 <210> SEQ ID NO: 13
166 <211> LENGTH: 5
E--> 167 <212> TYPE: Protein
168 <213> ORGANISM: Peptide
170 <220> FEATURE:
171 <223> OTHER INFORMATION: Aspergillus fumigatus
173 <400> SEQUENCE: 13
174 Thr Gly Glu Ser Leu
175 1       5
177 <210> SEQ ID NO: 14
178 <211> LENGTH: 6
E--> 179 <212> TYPE: Protein
180 <213> ORGANISM: Peptide
182 <220> FEATURE:
183 <223> OTHER INFORMATION: Aspergillus fumigatus
187 <400> SEQUENCE: 14
188 Cys Ser Asp Lys Thr Gly
189 1       5
191 <210> SEQ ID NO: 15
192 <211> LENGTH: 5
E--> 193 <212> TYPE: Protein
194 <213> ORGANISM: Peptide
196 <220> FEATURE:
197 <223> OTHER INFORMATION: Aspergillus fumigatus
199 <400> SEQUENCE: 15
200 Met Xaa Thr Gly Asp
```

L2127 Represents DNA|RNA|PRT
Invalid Response.
L2137 Responses can be either Artificial, Unknown or Genus Species. Pls see Err. 10 on Error Summary Sheet.
Same Error
Same Error

RAW SEQUENCE LISTING DATE: 05/17/2006
PATENT APPLICATION: US/10/822,235A TIME: 10:44:38

Input Set : A:\SEQLIST - text.txt
Output Set: N:\CRF4\05172006\J822235A.raw

201 1 5
203 <210> SEQ ID NO: 16
204 <211> LENGTH: 8
E--> 205 <212> TYPE: Protein
206 <213> ORGANISM: Peptide
208 <220> FEATURE:
209 <223> OTHER INFORMATION: Aspergillus fumigatus
211 <400> SEQUENCE: 16
212 Gly Asp Gly Xaa Asn Asp Xaa Pro
213 1 5
224 Attorney Docket Number: BSZ-049
226 -1-

Same Error

Same Error

Pls delete.

VERIFICATION SUMMARY DATE: 05/17/2006
PATENT APPLICATION: US/10/822,235A TIME: 10:44:39

Input Set : A:\SEQLIST - text.txt
Output Set: N:\CRF4\05172006\J822235A.raw

L:167 M:310 E: (3) Wrong or Missing Sequence Type, numeric identifier <212>, for SEQ ID#:13
L:179 M:310 E: (3) Wrong or Missing Sequence Type, numeric identifier <212>, for SEQ ID#:14
L:193 M:310 E: (3) Wrong or Missing Sequence Type, numeric identifier <212>, for SEQ ID#:15
L:205 M:310 E: (3) Wrong or Missing Sequence Type, numeric identifier <212>, for SEQ ID#:16